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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/265,710	03/09/1999	OLGA BANDMAN	PF-0339-1DIV	4844

27904 7590 07/26/2006

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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER
	20060721

DATE MAILED:

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Commissioner for Patents

See attached supplemental examiner's answer.

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER

Supplemental Examiner's Answer

Pursuant to the remand under 37 CFR 41.50(a)(1) by the Board of Patent Appeals and Interferences on 01 December of 2003 requiring a detailed response to the declaration under 37 C.F.R. § 1.132 by Lars Michael Furness that was filed on 19 February of 2002 a supplemental Examiner's Answer under 37 CFR 41.50(a)(2) is set forth below:

The declaration under 37 C.F.R. § 1.132 by Lars Michael Furness that was filed on 19 February of 2002 has not been previously answered at length because it does not appear to address any issues in dispute. The declaration shows that expression profiling for diagnostic and toxicology testing was a practice well known and established in the art prior to the filing of the instant application. Because the examiner does not dispute the existence and use of expression profiling techniques as well known research tools, there is little in the Furness declaration to answer. The only issue in dispute with respect to those arguments presented by Appellant that are based upon the Furness declaration is whether expression profiling is a specific and substantial utility for the claimed protein. Whereas the Furness declaration shows that expression profiling was a well-known and useful research tool at the time of the instant invention, it is noted that there were also many other well-known and indispensable research tools in use at that time, including other valuable analytical tools such as polyacrylamide gel electrophoresis (PAGE) and high performance liquid chromatography (HPLC). The need for a variety of different proteins in the practice of expression profiling is conceded, as is the need for various proteins or other compounds of different and known sizes to

serve as molecular weight markers in PAGE and HPLC. The issue in disputed in the instant appeal with regard to the Furness declaration is whether the employment of the claimed polypeptide of the instant application as a marker in expression profiling constitutes a specific and substantial utility for that protein that was well established at the time of the instant invention and, if so, does that utility differ from one which merely employs that same protein, or any protein having a known molecular weight, as a molecular weight marker in PAGE or any other analytical process? This appears to be a question of law, not a question of fact that can be resolved with a declaration under 37 C.F.R. § 1.132.

In Appellant's response of 28 February of 2002 to the non-final office action that was mailed 16 August of 2001, a Declaration under 37 C.F.R. § 1.132 by Lars Michael Furness was provided in support of Appellant's arguments that the claimed isolated polypeptide had practical uses in gene and protein expression monitoring applications as they would have been understood at the time of the filing of the instant patent application (third paragraph on page 7 of the response filed 28 February of 2002).

In the third paragraph on page 5 of Appellant's Brief, filed 03 September of 2002, Appellant argues that according to the Declaration, a person skilled in the art would have understood the claimed polypeptide, comprising the amino acid sequence of SEQ ID NO: 1, to be useful for a number of gene and protein expression monitoring applications, e.g. in the use of 2d gels and western blot analysis. Appellant further argues that, as demonstrated by the Furness Declaration (Dec. at ¶¶10-13), the person of ordinary skill in the art can achieve beneficial results from the claimed polypeptide in

the absence of any knowledge as to the precise function of that polypeptide. The Furness Declaration asserts that the claimed invention has specific, substantial, real-world utility by virtue of its use in toxicology testing, drug development and disease diagnosis through gene expression profiling.

The question at issue is whether or not the broad general assertion that the claimed isolated polypeptide, or any naturally occurring protein for that matter, might be used for some diagnostic application, in the absence of a disclosure that identifies a particular disease or disorder to be diagnosed through the detection of that isolated polypeptide, would be considered a specific, substantial, and credible utility for that polypeptide. The disclosure that any naturally occurring human protein, including the isolated polypeptide of the instant claims, can be employed in such an application does not satisfy the requirement of the statute that the claimed invention have at least one specific and substantial utility in currently available form. Expression profiling is not specific to the claimed polypeptide or a substantial use thereof because that process does not require the claimed invention since it can be practiced with essentially any diverse array of human proteins and the particular advantages of including a protein of the instant invention in that process are not disclosed in the instant specification. Again, it is unclear how the employment of the claimed polypeptide in this capacity differs from its use as a molecular weight marker in PAGE.

Appellant argues, and cites the Furness Declaration (Dec. at ¶ 10, Brief at pages 5 to 6) as evidence that toxicology testing is a well-established utility and concludes that the claimed polypeptides could be used in this manner and, therefore, that the claimed

invention possesses utility. However, for a "well-established" utility to satisfy the statutory requirements for patentability of a claimed invention, it must be specific to the claimed subject matter, it must be substantial and it must be credible. In this case all nucleic acids and genes are in some combination useful in toxicology testing. However, the particulars of toxicology testing with SEQ ID NO: 1 are not disclosed in the instant specification or the art of record. Neither the toxic substances nor the susceptible organs or systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID N0: 1. Because of this, such a utility is not specific to the claimed subject matter and does not constitute a "well-established" utility therefore. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in a practical form. Moreover, use of the claimed polypeptide in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of that array. Again, this is a utility that would apply to virtually ever member of a general class of materials, such as any collection of different proteins or DNA molecules from a single species of organism. Even if the level of expression of Appellant's individual polypeptide is affected by a test compound in an array that is being employed for drug screening, the specification does not disclose any specific and substantial interpretation for this result, and none is known in the art. Given this consideration, the individually claimed polypeptide has no "well-

established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what use any expression information regarding this polypeptide could be put.

Appellant has further relied upon the Furness declaration to support the argument that the claimed polypeptide has numerous practical, beneficial uses in drug development and the diagnosis of disease, none of which requires a detailed knowledge of how the polypeptide works.

With regard to drug discovery and development, (Dec. at ¶¶ 10-13, Brief at 9-10) Appellant mentions expression profiling as one use of the claimed polypeptide in the instant application. Appellant states that expression profiling is a method for identifying drug targets and characterizing diseases. Such a profile is independent of the function of the genes or gene products. In the instant case, the claimed polypeptide can be used as one of many targets on a microarray to generate an expression profile. A transcript image thus generated from lung tumor tissue can be compared, for example, with that from lung tumor tissue treated with a potential therapeutic compound in order to evaluate the efficacy of the compound.

However, there is no way to assess the meaning of any individual hit obtained from such a procedure. The first requirement is that one must know the biological significance of the polypeptide that is being evaluated. Without this information, the results of the expression profile are useless as they relate to that particular polypeptide because one would not know if the expression of that polypeptide should be increased

or decreased or even what significance could be attributed to such changes in an expression profile.

Appellant further argues, citing the Furness Declaration (Dec. at ¶10-13, Brief at 9) the utility of the claimed polypeptide in the diagnosis of disease. However, in order for a polypeptide to be useful for the diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a specific disease or disorder. The simple presence of a particular polypeptide in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polypeptide and that disease. If a molecule is to be used as an indicator of a disease state, there must be an established association between the level of expression of that molecule and the presence of a specific disease. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many thousands of proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is either present only in cancer tissue to the exclusion of normal tissue or it is expressed at higher or lower levels in diseased tissue as compared to normal tissue (i.e. overexpression or underexpression). Evidence of a differential expression pattern might serve as a basis for use of the claimed polypeptide as a diagnostic for the presence of a disease or disorder in an organism. However, in the absence of any disclosed relationship between the claimed polypeptide and any particular disease or disorder and the lack of any correlation between the claimed

polypeptide with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Congress intended that no patent be granted on a chemical compound whose sole utility consists of its potential role as an object of use-testing. Brenner 148 USPQ at 696. The disclosure does not present a substantial utility that would support the "useful" requirement of 35 U.S.C. § 101, as that requirement has been interpreted by the courts.

The Furness Declaration sets forth (Dec. at ¶10) that gene and protein expression monitoring applications are well-established utilities, that the claimed polypeptides could be used in this manner and that, therefore, the claimed invention possesses utility. However, for "well-established" utility to meet the "useful" requirement of 35 U.S.C. § 101 it must be specific, substantial and credible. In this case all nucleic acids and proteins comprising naturally occurring sequences are in some combination useful in expression monitoring. However, the particulars of monitoring the expression of a polypeptide comprising the amino acid sequence presented in SEQ ID NO: 1 of the instant application are not disclosed therein or in the prior art of record. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNAs from a particular species of organism, but is only potential with respect to SEQ ID N0: 1. Because of this, such a utility is not specific to the claimed subject matter and does not constitute a "well-established" and substantial utility for that particular protein. Further, because any potential diagnostic, toxicological or physiological association with the

claimed protein is not disclosed and has yet to be established, that protein does not have a specific and substantial utility in currently available form.

Moreover, as indicated above, the use of the claimed polypeptide in an array for expression monitoring is only useful in the sense that the information that is gained from an array comprising that polypeptide is dependent on the pattern derived from the array, and says, nothing with regard to each of the individual members of the array. Again, this is a utility that would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNAs from a single species of organism. Even if a test compound in an array for drug screening affects the expression of Appellant's individual polypeptide, the specification does not disclose any specific and substantial interpretation for the result, and none is disclosed in the prior art of record. Given this consideration, the individually claimed polypeptide has no "well-established" specific and substantial use. The artisan is required to perform further experimentation on the claimed material itself in order to discover to what use any expression information regarding this polypeptide could be put. It is a matter of law that an invention must have a specific and substantial utility "in currently available form", which precludes the need for further research, if that research is needed to establish a utility for the claimed invention (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)).

The appellant must within **TWO MONTHS** from the date of the supplemental examiner's answer exercise one of the following two options to avoid *sua sponte* **dismissal of the appeal** as to the claims subject to the rejection for which the Board has remanded the proceeding:

(1) **Reopen prosecution.** Request that prosecution be reopened before the examiner by filing a reply under 37 CFR 1.111 with or without amendment, affidavit, or other evidence. Any amendment, affidavit, or other evidence must be relevant to the issues set forth in the remand or raised in the supplemental examiner's answer. Any request that prosecution be reopened will be treated as a request to withdraw the appeal. See 37 CFR 41.50(a)(2)(i).

(2) **Maintain appeal.** Request that the appeal be maintained by filing a reply brief as set forth in 37 CFR 41.41. If such a reply brief is accompanied by any amendment, affidavit or other evidence, it shall be treated as a request that prosecution be reopened under 37 CFR 41.50(a)(2)(i). See 37 CFR 41.50(a)(2)(ii).

Extensions of time under 37 CFR 1.136(a) are not applicable to the **TWO MONTH** time period set forth above. See 37 CFR 1.136(b) for extensions of time to reply for patent applications and 37 CFR 1.550(c) for extensions of time to reply for ex parte reexamination proceedings.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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